REMARKS/ARGUMENTS

This amendment is filed in response to the Official Action mailed June 14, 2007 for this application. Reconsideration and further examination are respectfully requested.

The indication that claims 9, 11, 29, 30, 33 and 34 are allowable is noted with appreciation.

The Examiner objected to claims 35 to 37 as duplicates of claims 9-11. Claims 9-11 have been amended to clarify that "has the sequence" was intended to mean "consists of the sequence" consistent with ordinary English usage. In contrast, claims 35 to 37 refer to the use of antisense oligonucleotides is that are complementary to a region of the TRPM-2 mRNA that is also complementary to SEQ ID NO: 4, 5 or 12. These claims are therefore not identical.

The Examiner has made an obviousness-type double patenting rejection of claims 38 and 39 over US Patent Application No. 09/967,726. Since the present application is the earlier filed of the applications and since a terminal disclaimer has been filed in the other case to assure that common ownership will be maintained, there is no equitable reason for this rejection.

Claims 6, 8, 10, 12-17, 31 and 32 stand rejected under 35 USC § 103 as obvious over the Bruchovsky, in view of Sensibar, Kyprianou and Raghavan.

In the Official Action mailed November 14, 2006, the Examiner stated that Bruchovsky taught that "androgen withdrawal is routine treatment for prostate cancer and [provides] the suggestion to combine this with TRPM-2 gene therapy, a therapy known in the art as evidenced by the teachings of Sensibar." Applicants understood this to be an assertion that Sensibar teaches gene therapy, which it manifestly does not do. Now, in the Advisory Action, the Examiner states that Sensibar is only offered for a teaching of antisense inhibition of TRPM-2. The Examiner further asserts in the Advisory Action that "antisense inhibition of gene expression is a type of gene therapy." Applicants submit that key to this argument is any understanding in the art that the stated inhibition would be **therapeutic,** that is that it would provide any discernable benefit to a patient. This understanding is lacking. As previously noted, in the Sensibar paper, the LNCaP cells are first transfected to introduce a vector that will lead to TRPM-2 (SGP-2, clusterin) expression so that the effect of suppressing this expression can be observed. There is no teaching or suggestion in the paper of a therapeutic use of reducing TRPM-2 expression.

Now in this action, the Examiner cites two new references which are included "to include further teaching of gene therapy." (Office Action, Page 9). These references are generalized teachings with respect to gene therapy, which the Examiner offers as a teaching that antisense can be useful in gene therapy. These references in no way bridge the gap that they are offered

for, because they do not teach or suggest that TRPM-2 targeted antisense would be a type of antisense useful in gene therapy.

Furthermore, the suggestion in Bruchovsky upon which the Examiner relies is a suggestion of future experiments, no a predictor of outcome nor a suggestion of result. As inventor Martin Gleave has stated in a declaration filed in this case:

> The passage to which the Examiner refers is in a section of the paper entitled "Future Directions." At the time Bruchovsky et al. was written, we, as the authors of the paper, intended this as an indication of the direction that our research would take, and not as a statement that anti-TRPM-2 would necessarily provide a therapeutic benefit. Further, as a researcher studying this area, I would not understand this passage to provide an expectation of any particular result from the proposed experiments once performed. At that time, it simply was not known whether a decrease in TRPM-2 levels would cause or prevent apoptosis.

The Examiner asks clarification with respect to this argument because since "the instant claims only recite that TRPM-2 expression is reduced, the relevance of whether or not the effect of TRPM-2 expression on apoptosis was known prior to the time of filing is not understood."

The understanding in the art as to the effect of TRPM-2 expression or the reduction thereof is an absolutely essential component to any conclusion of obviousness. If the art as a whole teaches there is protein (TRPM-2) whose expression can be reduced by an antisense, this s not enough to create a reason to do this reduction in a therapeutic environment, or in the contraxt of a specific disease. If reduction of TRPM-2 causes apoptosis, this would be a good thing for therapy. But if it prevented apoptosis, it would be a bad thing.

The claims in this case refer to methods for treating prostate cancer ... not merely to methods for reducing expression of TRPM-2. The benefits with regard to treatment of prostate cancer is a consequence of the reduction in TRPM-2 expression, but nothing in the art supports a conclusion that such a benefit was a necessary result of the change in expression and therefore nothing in the art suggests or renders obvious the method of treatment.

With respect to claims 12, 13, 16, 17, 29, 30, Applicants again submit that the specification and the declaration evidence establishes the unexpected synergy that results from the combination of anti-TRPM-2 antisense and chemotherapy agents. The cited references Raghavan and Bruchosky do not show such a combination, and while they show other combinations these teachings do not suggest the synergy. Thus, this is an unexpected result which renders these claims patentable.

Furthermore, Applicants point out that the Examiner has read considerably more into the Kyprianou reference than is actually there. The Examiner argues that this reference teaches that "Bcl-2 expression is prostate tumors is associated with progression to androgen independence". What the reference actually says is that

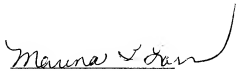
> "In the normal prostate gland, bcl-2 is expressed in the self-renewing, androgen-independent basal cells...
>
> "Augmented bcl-2 expression in malignant prostate epithelial cells is strongly associated with progression to androgen independent prostate cancer and poor prognosis (McDonnell et al., 1992; Colombel et al., 1993; Furuya et al., 1996). While bcl-2 expression has been associated with poor response to chemotherapy in acute myeloid leukemia (Campos et al., 1993) and breast cancer (Gasparini et al., 1995), the effect of bcl-2 over-expression on the therapeutic response of prostatic cancer remains to be investigated."

Taken as a whole, this is not the same as "teaching that Bcl-2 expression in prostate tumors is associated with progression to androgen independence", which implies a cause and effect, but is merely a teaching of an observation.

Finally, while the Examiner has rejected claim 8 as obvious over the cited art, there is no explanation as to why the limitation of claim 8 is taught or suggested by this art. This claim requires that the antisense overlap with the translation initiation or termination site in the particular TRPM-2 target. While some antisense that is effective against other targets may span initiation or termination, this is not universally the case, and the structure of these sites needs to be looked at in determining if such a cite is obvious. Thus, the Examiner has presented no prima facie case with respect to claim 8.

For these reasons, Applicants submit that all of the pending claims are now in form for allowance. Favorable reconsideration and allowance of all claims are respectfully urged.

Respectfully submitted,



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